JOURNAL OF PURE AND APPLIED MICROBIOLOGY, Dec. 2017. Vol. **11**(4), p. 1851-1854

Blood-Stream Infection among Chronic Hemodialysis Patients: Review Article

Shaima M.Alhazmi and Samah O. Noor

Department of Biology, Faculty of Science, King Abdulaziz University, Jeddah, Saudi Arabia.

http://dx.doi.org/10.22207/JPAM.11.4.25

(Received: 10 November 2017; accepted: 09 December 2017)

The susceptibility to infection among dialysis patients usually associated with the dialysis procedure itself.Hemodialysispatients require a vascular access that can be punctured to remove and replace blood, these vascular accesses listed in order as a major cause of infections.

Keywords: Dialysis;hemodialysis; Bloodstream infection; End-stage renal disease; risk factor.

There are many complications of dialysis treatment, some of them lead to a high morbidity and mortality. The annual mortality rate in hemodialysis (HD) patients is 23%, and the infection is the second most common cause of death, it accounts for nearly 14% of the mortality cases[1]. According to the United States Renal Data System (USRDS) registry: "Infection is the second leading cause of death in patients with end-stage renal disease (ESRD)"[2].

The infection occurs when microorganisms invade the body, causing tissue damaged and resulting signs or symptoms of infection[1]. The incidence of infections in dialysis settings is increasing while declined in other healthcare settings[3]. It is common and real difficult health problem in patients undergoing dialysis and represents as clinical challenge at dialysis units.

It is well known that dialysis patients are immunocompromised, and they are susceptible to infections because of multiple co-morbidities and many factors that depressing their immune systems, thus, a high rate of infection among them are expected. The susceptibility to infection among these patients usually associated with the dialysis procedure itself, they are highly exposed to infections that are easily transmitted through blood during dialysis procedure. Hemodialysis patients require a vascular access that can be punctured to remove and replace blood, these vascular accesses listed in order as a major cause of infections.

Vascular access types and the insertion and maintenance practices act as a portal of entry for organisms, and are associated with the majority ofblood-stream infections (BSIs) in HD population. According to the Centers for Diseases Control and Prevention (CDC)[3], in US during 2008, an estimated 37,000 BSIs related to central lines occurred among HD patients.

During normal course of HD procedure patients are exposed to several infection risks; potential sources of infection include the skin (through repeated disruption of the skin barriers and integrity by the vascular access), contamination of dialysis equipment and medication vails and inadequate dialyzer reuse[4]. Other risk factors include old age, severity of illness, long-term hospital stay, repeated antibiotic treatment and specific immune system defects associated with renal dysfunction[5].

Based on the USRDS annual reports, one of the main cause of morbidity events among patients receiving renal replacement therapy is

* To whom all correspondence should be addressed.
E-mail: sonoor@kau.edu.sa

hospitalization for infection, which increased by 43% from 1993 to 2011[6], that making infection is the leading cause of hospitalization and the second leading cause of death among dialysis patients[7].

As a result of frequent hospitalization and repetitive exposure to healthcare environments, HD patients are susceptible to nosocomial infections. They are exposed to antibiotic-resistant pathogens due to treated frequently with long courses of antimicrobials[8]. Another report of USRDS showed that there is an increase in the rate of infection-related hospitalizations of HD patients while there is a fall in the rate for other disorders, that suggests there is an urgent need for effective strategies to prevent dialysis-related infections[9].

On the other hand, infection among HD patients results in major medical complications, long hospital stay and high economic burden. It has been estimated that the cost per infection is $34,508 - $56,000[2]. Intervention strategies focused on infection prevention specially with increasing microorganism resistance and challenges of newly discovered antibiotics.

The number of patients undergoing dialysis is increasing each year, and the higher prevalence of infections among them is still observed. In the United States during 2004, there were 309,269 patients received treatment for ESRD only by HD technique[10].

Blood-stream Infection (BSI)

Patients with ESRD on HD are at a greater risk for bacterial infection. Bacterial pathogens are well recognized as an important cause of morbidity and mortality among HD patients. Blood-stream infection defined as a positive blood culture result that is verified presence of bacteria and/or fungi in the blood[11].

Blood-stream infection can be either exogenous (i.e., from contaminated dialysis fluids or equipment) or endogenous (i.e., by bacteria present in or on the patient). Exogenous bacteria have caused numerous outbreaks in HD units, most of these outbreaks resulted from inadequate dialyzer reprocessing procedures, or contaminated water using in dialysis, or contaminated medication vials[1].

Rates of BSI in patients undergoing HD appear to vary depending on type of vascular access that is applied. According to North American data, the rate of BSI in HD patients varied depending on type of vascular access used range between 0.5 and 27.1 per 100 patients/month[12]. Compared with fistula, the use of catheter associated with an increase the risk up to 10 times[13]. Catheter-related infection is one of the most common forms of bacterial infection in patients receiving HD[14]. Data in the literature have shown high morbidity and mortality rates linked to BSIs among patients who used catheters for HD.

Patients dialyzed through catheters are at high risk of endogenous BSI by Staphylococci, particularly, *Staphylococcus aureus*. The skin and hubs of the catheters are the most frequent sources of colonization risk. Catheters get colonized either through extra-luminal (skin-related) or intra-luminal (hub-related) routes. The first case, migration of bacteria from skin through the insertion site along the catheter, finally bacteria reach to the blood stream. In the second case, the catheter hub is contaminated during catheter manipulation and maintenance by dialysis personnel, the colonized bacteria then spread through the lumen of the catheter causing BSI[15]. The adherence properties of bacteria are important determinants of catheter-related infection, for example, *S. aureus* adheres to host proteins that are commonly present on catheters, such as fibrinogen, whereas coagulase-negative staphylococci directly adhere to the catheter's surface[4].

One of the factors that complicate the infection treatment of patients with catheters is a biofilm formation in the catheter lumen. Biofilm formation makes bacteria 100-1,000 times less susceptible to antibiotics and becoming more resistant to the antimicrobial mechanisms compared with free-growing bacteria (planktonic)[13,16]. Usually catheter removal is often the only option to eradicate the infection. Therefore, much of the research has been focused on prevention of catheter colonization[17].

Among the microorganisms responsible for BSI in HD patients; gram-positive bacteria are the most common organisms causing bacteremia. However, BSI may also be caused by gram-negative pathogens[18]. The most gram-positive organisms that associated with HD infections are *S. aureus* and coagulase-negative staphylococci[16].

In a study by National Health Safety Networks (NHSN), the data were collected from 461 catheter-related BSIs showed that 19.7% were

by *S. aureus*, while 46% were by other Gram-positive organisms. Gram-negative bacilli were caused approximately 23.2% of infections, while 1.7% of cases were by fungi[19]. In the U.S. during 2006, 32 providers of HD outpatient voluntarily reported 3,699 adverse events to the CDC, the findings showed that among 599 isolates reported, 461 (77%) represented catheter-related BSIs, and 138 (23%) were in patients with fistulas or grafts. The most microorganisms frequently identified were common skin contaminants such as coagulase-negative staphylococci[10].

According to U.S. data, coagulase-negative staphylococci are found in 32-45% of BSI cases, *S. aureus* in 22-29% and *Enterococci* in 9-13% of cases, while Gram-negative bacteria was isolated in 21-30% of cases. The type of microorganism isolated seems dependent on the type of vascular access used, S. aureus rate was higher with fistulas and grafts, while coagulase-negative *staphylococci* and Gram-negative bacteria were higher in patients with catheters. Furthermore, HD patients have an increased risk of infections with multidrug-resistant organisms (MDROs), such as Methicillin-resistant *Staphylococcus aureus* (MRSA)[13].

Patients undergoing HD are generally susceptible to infections caused by MDROs due to frequent exposure to health care settings, multiple hospitalizations or surgical procedures, and they are often treated with long courses of antimicrobials[1]. Data analysis from the CDC-funded surveillance system for invasive MRSA infections, Lucero and his colleagues found that the risk for invasive MRSA infections in HD patients was higher more than 100 times than for the general population[9].

Methicillin-resistant *S. aureus* BSI has been a cause of major concern in healthcare systems worldwide, because of its high incidence rates and undesirable related outcomes. Most series have found that the most frequent source of MRSA-BSI was the catheter[20].

There are still large gaps in the understanding of the transmission approaches of MDROs in outpatient HD facilities. In addition to Infection control practices, the judicious use of antimicrobial agents should be followed strictly as effective means to limit prevalence of these organisms[9].

Management of BSIs in HD patients is complicated due to the limited vascular access options[16]. Treatment with systemic antibiotics should be prescribed before blood culture results without delay. The initial empiric antibiotic should be covering both gram-positive and gram- negative bacteria[13].

Monitoring infections among dialysis patients is an important component of improving dialysis outcomes. the CDC in 1999, initiated the Dialysis Surveillance Network; a surveillance system that available to all centers caring for outpatients undergoing HD[21]. Surveillance data collected at the facility level (local level, i.e., center-specific) can help to identify areas where improvements in infection control might be necessary[2], and following these events overtime to evaluate the effectiveness of prevention and interventions, and compare the findings with other, similar facilities[9].

Several infection control practices have been recommended to decrease BSIs in HD patients, especially those with central venous catheters; these include hand hygiene should always be practiced both by patients and by health care providers prior to contact with vascular access exit site, optimal vascular access insertion practices, the use of 2% chlorhexidine for skin antisepsis and the use of antimicrobial ointments at the catheter site[4]. Patient on HD are the key partner in BSI prevention; the CDC has published a list of recommendations for prevention of BSIs among patients on dialysis, which includes that providing standardized education on infection prevention topics to all patients, hand hygiene, vascular access care and managements when patients away from the dialysis unit, the risks related to catheter use, and recognizing signs of infection[22].

CONCLUSIONS

Type of vascular access represent the main risk factor associated with BSI in patients undergoing HD, and it still has a strong influence the clinical outcomes of HD treatment. Arteriovenous fistula is the best available option for HD patients, and have a much lower infection ratecompared to central venous catheter. A reduction in the number of infections is critical in HD population and can

be achieved by increasing the use of fistula and decreasing the use of catheter.

REFERENCES

1. CDC (2001) Recommendations for Preventing Transmission of Infections Among Chronic Hemodialysis Patients. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5005a1.htm [accessed 16.11.24].
2. Zhang J, Li R, Chen K, Ge L, Tian J, Antimicrobial lock solutions for the prevention of catheter-related infection in patients undergoing haemodialysis: study protocol for network meta-analysis of randomised controlled trials. *BMJ Open,* 20016; **6**(1):e010264.
3. CDC. Reducing Bloodstream Infections in an Outpatient Hemodialysis Center — New Jersey, 2008–2011. MMWR: Morbidity and Mortality Weekly Report, 2012; **61**(10):169-173.
4. JABER B. Bacterial infections in hemodialysis patients: Pathogenesis and prevention. *Kidney International*, 2005; **67**:2508–2519.
5. Diawara I, Bekhti K, Elhabchi D, Saile R, Elmdaghri N, Timinouni M et al. *Staphylococcus aureus* nasal carriage in hemodialysis centers of Fez, Morocco. IRAN. J. MICROBIOL, 2014; **6**(3):175-183.
6. Fram D, Taminato M, Ponzio V, Manfredi S, Grothe C, Batista R et al. Risk factors for morbidity and mortality of bloodstream infection in patients undergoing hemodialysis: a nested case–control study. *BMC Research Notes,* 2014; **7**(1):882.
7. Abdelsatir S. Evaluation of Nurses Awareness and Practice of Hemodialysis Access Care in Khartoum State, Sudan. *Arab Journal of Nephrology and Transplantation,* 2013; **6**(2):119-21.
8. Klevens R, Tokars J, Andrus M. Electronic reporting of infections associated with hemodialysis. *Nephrology news & issues,* 2005; **19**(7):37-38,43.
9. Kallen A J, Arduino M J, Patel P R. Preventing Infections in Patients Undergoing Hemodialysis. *Expert Reviews Anti-infective Therapy,* 2010; **8**(6): 643-655.
10. Klevens RM, Edwards JR, Andrus ML, Peterson KD, Dudeck MA, Horan TC; NHSN Participants in Outpatient Dialysis Surveillance. Dialysis Surveillance Report: National Healthcare Safety Network (NHSN)-data summary for 2006. *Semin Dial,* 2008; **21**(1): 24-28.
11. Dalgaard L, Nørgaard M, Jespersen B, Jensen-Fangel S, Østergaard LJ, Schønheyder HC, Søgaard O. Risk and Prognosis of Bloodstream Infections among Patients on Chronic Hemodialysis: A Population-Based Cohort Study. *PLoS ONE,* 2015; **10**(4): e0124547.
12. Fram D, Okuno M, Taminato M, Ponzio V, Manfredi S, Grothe C et al. Risk factors for bloodstream infection in patients at a Brazilian hemodialysis center: a case–control study. *BMC Infectious Dis,* 2015; **15**(1).
13. Böhlke M, Uliano G, Barcellos F. Hemodialysis catheter-related infection: prophylaxis, diagnosis and treatment. *The J of Vascular Access,* 2015; **16**(5):347-355.
14. Lata C, Girard L, ParkinsM and James M. Catheter-related bloodstream infection in end-stage kidney disease: a Canadian narrative review. *Canadian Journal of Kidney Health and Disease,* 2016; **3**: 24.
15. Saxena A &Panhotra B. Haemodialysis catheter-related bloodstream infections: current treatment options and strategies for prevention. SWISS MED WKLY, 2005; **135**: 127–138.
16. Fitzgibbons L, Puls D, Mackay K and Forrest G. Management of Gram-Positive Coccal Bacteremia and Hemodialysis. *Am J Kidney Dis,* 2011; **57**(4):624-640.
17. Saxena A, Panhotra B, Al-Mulhim A. Vascular Access Related Infections in Hemodialysis Patients. *Saudi J Kidney Dis Transplant,* 2005; **16**(1): 46-71.
18. Fysaraki M, Samonis G, Valachis A, Daphnis E, Karageorgopoulos D, Falagas M et al. Incidence, Clinical, Microbiological Features and Outcome of Bloodstream Infections in Patients Undergoing Hemodialysis. *Int J of Med Sci,* 2013; **10**(12):1632-1638.
19. Soi V, Moore C, Kumbar L, Yee J. Prevention of catheter-related bloodstream infections in patients on hemodialysis: challenges and management strategies. *International Journal of Nephrology and Renovascular Disease*, 2016; **9**: 95–103.
20. Cuervo G, Camoez M, Shaw E, Dominguez M, Gasch O, Padilla B et al. Methicillin-resistant Staphylococcus aureus (MRSA) catheter-related bacteraemia in haemodialysis patie*nts. BMC Infectious* Dis, 2015; **15**(1):484.
21. Tokars J, Miller E, Stein G. New national surveillance system for hemodialysis-associated infections: Initial results**.** *Am J Infect Control,* 2002; **30**(5):288-95.
22. See I, Shugart A, Lamb C, Kallen A, Patel P, Sinkowitz-Cochran R. Infection Control and Bloodstream Infection Prevention: The Perspective of Patients Receiving Hemodialysis. *NephrolNurs J,* 2014; **41**(1): 37–40.